General

Guideline Title

United Kingdom national guideline for the management of donovanosis (granuloma inguinale) 2011.

Bibliographic Source(s)

Clinical Effectiveness Group. United Kingdom national guideline for the management of donovanosis (granuloma inguinale) 2011. London (UK): British Association for Sexual Health and HIV; 2011. 7 p. [21 references]

Guideline Status

This is the current release of the guideline.

This guideline updates a previously released version: Association for Genitourinary Medicine (AGUM), Medical Society for the Study of Venereal Disease (MSSVD). 2002 national guideline for the management of donovanosis (granuloma inguinale). London: Association for Genitourinary Medicine (AGUM), Medical Society for the Study of Venereal Disease (MSSVD); 2002. Various p. [21 references]

Regulatory Alert

FDA Warning/Regulatory Alert

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- May 12, 2016 – Fluoroquinolone Antibacterial Drugs : The U.S. Food and Drug Administration (FDA) is advising that the serious side effects associated with fluoroquinolone antibacterial drugs generally outweigh the benefits for patients with sinusitis, bronchitis, and uncomplicated urinary tract infections who have other treatment options. For patients with these conditions, fluoroquinolones should be reserved for those who do not have alternative treatment options.

Recommendations

Major Recommendations

Levels of evidence (I-IV) and grades of recommendation (A-C) are defined at the end of the "Major Recommendations" field.

Diagnosis

The main method of diagnosis is the demonstration of Donovan bodies in either:

- Cellular material taken by scraping/impression; smear/swab/crushing of pinched off tissue fragment on to glass slide
  or
- Tissue sample collected by biopsy

Smears can be stained with Giemsa, Wright's stain, or Leishman stain. Biopsies are best stained with silver stains (for example, Warthin-Starry) or Giemsa. Donovan bodies are characterised by:

- Location within large (20-90 μm) histiocytes
- Pleomorphic appearance 1-2 x 0.5-0.7 μm
- Bipolar densities and a capsule often visible
- Stain Gram-negative

Expert opinion has estimated that in endemic areas identification of Donovan bodies is achievable in 60% to 80% of patients considered to have donovanosis on clinical grounds.

Successful culture of the causative organism, *Klebsiella granulomatis*, has recently been reported in human peripheral blood monocytes and in HEp-2 cells. Both polymerase chain reaction (PCR) methods and serological tests for donovanosis have been described but are not yet routinely available.

Management

All patients with active lesions shown to contain Donovan bodies should receive antimicrobial treatment. Patients from areas endemic for donovanosis with a clinical diagnosis of the disease should be given presumptive treatment.

Treatment options are presented in the table below, which lists drugs shown to be effective in the treatment of donovanosis in prospective studies. Drugs have been selected on the basis of current availability, lack of major toxicity, and convenient dosage regimens. Older drugs known to be effective but not included are trivalent antimonials, streptomycin, chloramphenicol, thiamphenicol, chlortetracycline, and oxytetracycline. Ampicillin has been omitted because of conflicting data on efficacy. Recent experience with azithromycin in Australia has been so encouraging in all categories of patient that a proposal to eradicate donovanosis by the year 2003 in Australia has been formally adopted.

Table: Drugs Shown to be Effective in the Treatment of Donovanosis

Drug	Dose	Route	Grading of Recommendation	Level of Evidence
Azithromycin	1 g weekly or 500 mg daily	Oral	B	Ib
Ceftriaxone	1 g daily	Intramuscular (IM)/Intravenous (IV)	B	IIb
Co-trimoxazole*	160/800 mg twice daily	Oral	B	IIb
Doxycycline*	100 mg twice daily	Oral	C	IV
Erythromycin*	500 mg four times daily	Oral	C	IV
Norfloxacin	400 mg twice daily	Oral	B	IIb
Gentamicin*	1 mg/kg every 8 hours	IM/IV	C	III

*Currently recommended by the U.S. Centers for Disease Control and Prevention (CDC).

Notes on the Table

Azithromycin is recommended for donovanosis in the Australian Antibiotic Guidelines.
The CDC recommends ciprofloxacin which has better bioavailability than norfloxacin.
Gentamicin is recommended by the CDC as an adjunct to therapy in patients whose lesions do not respond in the first few days to other

agents.

Doxycycline has not been individually assessed prospectively and recommendations are based on trials carried out with older tetracyclines (oxytetracycline, chlortetracycline, etc.) which are assumed to be equivalent to doxycycline, which is chosen for more convenient twice daily dosing.

Duration of treatment should be until lesions have healed. Healing times vary greatly between patients. The CDC recommends a minimum of 3 weeks' treatment.

Treatment for Pregnant or Lactating Mothers

Gentamicin, doxycycline, co-trimoxazole, and norfloxacin are not recommended for pregnant or lactating women. Erythromycin has been used successfully in pregnant women with donovanosis. Children born to mothers with untreated genital lesions of donovanosis are at risk of infection and a course of prophylactic antibiotics should be considered.

Partner Management

Any person with a history of unprotected sexual contact with a patient with active donovanosis or within 40 days before the onset of lesions should be assessed clinically for evidence of infection and offered treatment. This recommendation is based on best estimates of the incubation period reported by one researcher who studied 60 patients and found an incubation period of between 3 and 40 days in 92% of patients.

Follow Up

Patients should be followed until symptoms have resolved.

Definitions:

Levels of Evidence

Level	Type of Evidence
Ia	Evidence obtained from meta-analysis of randomised controlled trials
Ib	Evidence obtained from at least one randomised controlled trial
IIa	Evidence obtained from at least one well-designed controlled study without randomisation
IIb	Evidence obtained from at least one type of well-designed quasi-experimental study
III	Evidence obtained from well-designed, non-experimental descriptive studies, such as comparative studies, correlation studies and case control studies
IV	Evidence obtained from expert committee reports or opinions and/or clinical experience of respected authorities

Grades of Recommendation

Grade	Recommendation
A (Evidence levels Ia, Ib)	Requires at least one randomised controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation
B (Evidence levels IIa, IIb, III)	Requires availability of well-conducted clinical studies but no randomised clinical trials on the topic of recommendation
C (Evidence level IV)	Requires evidence from expert committee reports or opinions and/or clinical experience of respected authorities. Indicates absence of directly applicable studies of good quality

Clinical Algorithm(s)

None provided

Scope

Disease/Condition(s)

Donovanosis (granuloma inguinale)

Guideline Category

Diagnosis

Evaluation

Management

Prevention

Treatment

Clinical Specialty

Infectious Diseases

Obstetrics and Gynecology

Urology

Intended Users

Physicians

Guideline Objective(s)

To offer recommendations on the diagnostic tests, treatment regimens and health promotion principles needed for the effective management of donovanosis (granuloma inguinale), covering the management of the initial presentation, as well as how to prevent transmission and future infection

Target Population

This guideline is aimed primarily at people aged 16 years or older (see specific British Association for Sexual Health and HIV [BASHH] guidelines for those under 16) presenting to health care professionals, working in departments offering Level 3 care* in STI management within the United Kingdom.

*The principles of the recommendations should be adopted across all levels (levels 1 and 2 may need to develop, where appropriate, local care pathways).

Interventions and Practices Considered

Diagnosis

1. Demonstration of Donovan bodies in:
    - Cellular material by scraping/impression smear/swab/crushing of pinched off tissue fragment on to glass slide
    - Tissue sample collected by biopsy
2. Culture of *Klebsiella granulomatis* in human peripheral blood monocytes and in HEp-2 cells

Note: Polymerase chain reaction methods and serological tests for donovanosis are considered but these tests are not yet routinely available.

Treatment/Management

1. Antimicrobial therapy:
    - Azithromycin
    - Ceftriaxone
    - Co-trimoxazole
    - Doxycycline
    - Erythromycin
    - Norfloxacin
    - Gentamicin
2. Older drugs known to be effective (e.g., trivalent antimonials, streptomycin, chloramphenicol, thiamphenicol, chlortetracycline, and oxytetracycline)
3. Prophylactic antibiotic for children born to mothers with untreated genital lesions
4. Partner management
5. Follow-up

Major Outcomes Considered

- Proper identification of Donovan bodies, particularly in endemic areas
- Potential complications of untreated infections, including vertical transmission

Methodology

Methods Used to Collect/Select the Evidence

Hand-searches of Published Literature (Primary Sources)

Hand-searches of Published Literature (Secondary Sources)

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

Information was obtained by searching the Cochrane Library and Medline databases and Google Scholar from 1966 up to February 2009 using the MeSH heading 'granuloma inguinale' and free text searching using 'granuloma inguinale', 'Donovanosis', and '*Calymmatobacterium granulomatis*' and '*Klebsiella granulomatis*'. EMBASE was searched from 1980 to Feb 2009. References of all retrieved articles were checked in order to identify additional material. *Index Medicus* from 1879 to 1965 was hand searched for all articles on granuloma inguinale by the author for an extended review of diagnosis and treatment of donovanosis published in 1991.

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Weighting According to a Rating Scheme (Scheme Given)

Rating Scheme for the Strength of the Evidence

Levels of Evidence

Level	Type of Evidence
Ia	Evidence obtained from meta-analysis of randomised controlled trials
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III	Evidence obtained from well-designed, non-experimental descriptive studies, such as comparative studies, correlation studies and case control studies
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Methods Used to Analyze the Evidence

Systematic Review

Description of the Methods Used to Analyze the Evidence

Not stated

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Not stated

Rating Scheme for the Strength of the Recommendations

Grades of Recommendation

Grade	Recommendation
A (Evidence levels Ia, Ib)	Requires at least one randomised controlled trial as part of the body of literature of overall good quality and consistency addressing the specific recommendation
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Cost Analysis

A formal cost analysis was not performed and published cost analyses were not reviewed.

Method of Guideline Validation

Not stated

Description of Method of Guideline Validation

Not applicable

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is graded and identified for select recommendations (see the "Major Recommendations" field).

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

Appropriate diagnosis and management of donovanosis

Potential Harms

Not stated

Contraindications

Contraindications

Gentamicin, doxycycline, co-trimoxazole, and norfloxacin are not recommended for pregnant or lactating women.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy is not provided.

Implementation Tools

Audit Criteria/Indicators

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

IOM Care Need

Getting Better

Staying Healthy

IOM Domain

Effectiveness

Identifying Information and Availability

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Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

1999 Aug (revised 2011)

Guideline Developer(s)

British Association for Sexual Health and HIV - Medical Specialty Society

Source(s) of Funding

British Association for Sexual Health and HIV

Guideline Committee

Clinical Effectiveness Group (CEG)

Composition of Group That Authored the Guideline

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Financial Disclosures/Conflicts of Interest

None

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Guideline Availability

Electronic copies: Available from the British Association for Sexual Health and HIV Web site .

Availability of Companion Documents

The following is available:

- British Association for Sexual Health and HIV: framework for guideline development and assessment. British Association for Sexual Health and HIV; 2010. 18 p. Electronic copies: Available in PDF from the BASHH Web site .

In addition, auditable outcomes are provided in the original guideline document .

Patient Resources

None available

NGC Status

This summary was completed by ECRI on June 15, 2000. The information was verified by the guideline developer on October 13, 2000. This summary was updated on June 24, 2002. This summary was updated by ECRI Institute on October 3, 2007 following the U.S. Food and Drug Administration (FDA) advisory on Rocephin (ceftriaxone sodium). This summary was updated by ECRI Institute on June 6, 2012. This summary was updated by ECRI Institute on October 25, 2013 following the U.S. Food and Drug Administration advisory on Fluoroquinolone Antibacterial Drugs. This summary was updated by ECRI Institute on May 18, 2016 following the U.S. Food and Drug Administration advisory on Fluoroquinolone Antibacterial Drugs.

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